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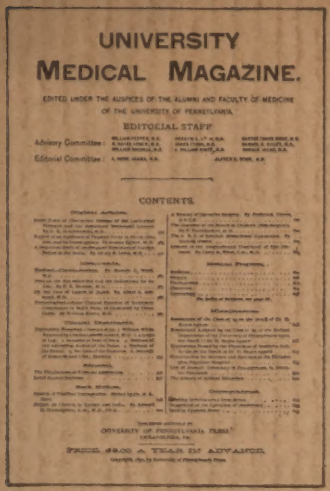

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ON POTASSIUM PERMANGANATE AS AN ANTIDOTE TO VEGETABLE POISONS.

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This paper is the outcome of an attempt at a research which has been aborted by multitudinous professional engagements, a tired nervous system, and the immediate approach of a European vacation. The results reached have seemed worthy of being put on record, even if they be not final, and be, as the author hopes, only the prelude of an elaborate study later in the year.

Dr. Johann Antal appears to be the first to have suggested the use of potassium permanganate as an antidote for vegetable organic poisons.[1] He experimented with *muscarine*, *strychnine*, *colchicine*, *oil of savine*, and *oxalic acid*. He found that if the solution of permanganate were given at the same time as the poison it prevented the action, although in control experiments the doses of poison were always fatal. He even found that no poisonous effect was produced by the hypodermic injection of strychnine, provided the permanganate was immediately injected into the same spot.

The next experimenters in this line were Schlagdenhauffen and Reeb, who studied the antidotal power of the poison upon the glucoside *coronillin*. They found that a dose of coronillin, which in the control experiment with a pigeon proved fatal, had no effect upon a second pigeon when mixed with a solution of the permanganate. Again, a mixture of the permanganate with the coronillin injected into the guinea-pig failed to act, although the same dose of coronillin given by itself killed a second guinea-pig. They further claim, it is not necessary that the permanganate be injected into the same position, or at the same time, as the coronillin, finding in a series of experiments upon frogs that even the distant injection of the permanganate suspends the action of the coronillin. They declare that the addition of the carbonate of soda, or any other alkaline salt, greatly hastens the action of the permanganate upon the coronillin.[2]

Dr. Wm. Moor[3] proposed the potassium permanganate as a chemical antidote for *morphine*. He states that if one grain of morphine sulphate be dissolved in a solution of 250 grains of white of egg and one ounce of water, and one grain of potassium permanganate dissolved in

[1] Magyar Orvosi Archivum, 1893, 2 Heft, Excerpt, but is known to me only by the excerpt in the Pesther medizinische chirurgische Presse, 1893.

[2] Journal de Pharmacie, October, 1893.

[3] New York Medical Record, February 17, 1894.

one ounce of water be added, the morphine will be immediately destroyed without the albumen being interfered with. As the result of a series of chemical experiments he comes to the conclusion that potassium permanganate has no effect upon atropine, cocaine, veratrine, pilocarpine, aconitine, or strychnine. In proof of the antidotal value of the permanganate, Dr. Moor himself took semipublicly three grains of morphine sulphate followed immediately by the permanganate. No narcotic effects were produced.

In approaching the practical study of the antidotal value of potassium permanganate, the subject naturally divides itself into two portions, first, as to the value of the permanganate when given by the mouth as a chemical antidote; second, as to the possibilities, as is alleged, of its following the poison into the blood, and there acting chemically upon it. In accordance with this division, I shall arrange my paper, so far as morphine is concerned, into two parts, Sections A and B.

MORPHINE.

Section A.

In testing the antidotal value of the permanganate I have made two series of experiments: first, those in which the permanganate solution was added to the alkaloidal solution outside of the body, the precipitate removed, and the filtrate given either by the mouth or hypodermically; second, those in which the two agents were given separately by the mouth. The experiments made with the filtrate were as follows:

SERIES I.

Experiment.	Animal.	Drug.	Result.	Remarks.
1	Pigeon	2.5 c.c., 8-per-cent. solution of morphine.	Death in twenty-two minutes.	Control experiment.
2	"	2.5 c.c.; eighteen minutes later a second 2.5 c.c. of filtrate.	No apparent illness.	
3	"	4 c.c. filtrate representing 5 c.c. morphine solution, 8 per cent.	No apparent illness.	
4	"	7 c.c. filtrate; 10 minutes later, 5 c.c. filtrate.	Died suddenly one hour and fifty minutes after filtrate.	No convulsions or other evidences of morphine-poisoning.

In making the experiments just given probably from five to ten minutes elapsed between the time at which the two solutions were poured together and that at which the finished filtrate was removed

from under the funnel, although the mixed solutions were poured upon the filter-paper within a minute of their original conjunction.

The result of the experiments seems to show that the filtrate from the mixed solution of potassium permanganate and morphine sulphate is almost, but not absolutely, devoid of poisonous properties. Twice the ordinary dose of the morphine solution failed to produce any symptoms, and when death did occur after an enormous dose of the filtrate the symptoms were not those of morphine-poisoning ; an indication that the result may have been produced by some substance other than the narcotic alkaloid.

I next attempted a series of experiments upon dogs with the morphine given by the mouth, but found the result very unsatisfactory. In a number of control experiments I failed entirely to kill the dog with morphine. Thus fifty cubic centimetres of a 4-per-cent. solution of morphine sulphate (representing 30.7 grains of alkaloidal salt) produced in a dog weighing ten kilos great quietude, with some stiffness and much evidence of illness, ending, however, in complete recovery ; and when I assayed larger doses vomiting came on in every case, and no symptoms of morphine-poisoning were produced. Two somewhat satisfactory experiments were made with the morphine solution in the rabbit. Ten cubic centimetres of a 4-per-cent. solution of morphine I found to cause in a rabbit weighing 3.25 pounds violent, persistent tetanus, beginning in fifteen minutes, but finally recovered from ; while in a second experiment with a rabbit weighing 3.50 pounds ten cubic centimetres of the narcotic solution, followed in six minutes by ten cubic centimetres of the potassium permanganate (4 per cent.), failed to produce any evidence of poisoning whatever.

From these few and inconclusive experiments it is evident that such enormous amounts of morphine are recovered from by the animal when the alkaloid is given by the mouth that antidotal experiments are very unsatisfactory. Under these circumstances chemical studies become of especial value. I am happy to be able to give the results of some very careful work by Professor Wormley.

Professor Wormley dissolved 250 milligrammes of morphine sulphate in 25 cubic centimetres of water containing 500 milligrammes of potassium permanganate ; maintained temperature at 100° C. for ten minutes, at end of which time color was discharged. The mixture was then treated with slight excess of ammonia and extracted with hot amylic alcohol ; the extract showed traces of morphine.

In conclusion, it seems to me that the evidence which has been offered by Dr. Moor and others, taken in conjunction with what I have been able to bring forward, indicates that the potassium permanganate given by the mouth directly after poisoning is a valuable, but not

perfect, antidote to the morphine salts; an antidote, however, which should not be relied upon to the exclusion of emptying the stomach by medicinal or mechanical means.

Section B.

I do not know that it has been claimed in type by any American observer that the potassium permanganate is capable of following an organic poison into the blood and there acting upon it, although I was recently surprised to find in New York City the wide-spread belief in the existence of such action, so that tablets of the potassium permanganate are furnished for hypodermic use. Further, Schlagdenhauffen and Reeb distinctly claim that the permanganate has the power of being absorbed and acting upon the poison which has been previously taken into the blood. The avidity with which potassium permanganate attacks all kinds of organic matters, living or dead, strongly militates against its capability of absorption into the blood, and I have always believed that such absorption was impossible. Nevertheless, it is necessary to test by experiment this *à priori* reasoning in order to arrive at positive conclusions. Experiments were therefore made upon pigeons in which a morphine sulphate and potassium permanganate were given hypodermically.

No.	Morphine solution, 8 per cent.	Permanganate solution, 4 per cent.	Result.
1 control	2.0 c.c.	None	Recovery.
2	2.0 c.c.	2 c.c.	Death in one hour and forty minutes.
3	2.0 c.c.	4 c.c.	Death in one hour and sixteen minutes.
4 control	2.5 c.c.	None	Death in twenty-two minutes; pigeon very young.
5 control	2.5 c.c.	None	Recovery after some tetanus; old pigeon.
6	2.5 c.c.	5 c.c.	Death in fifty six minutes.
7	2.5 c.c.	5 c.c.	Death; time not known.

Upon rabbits two experiments were performed with solutions and in a manner precisely like those just described.

No.	Weight.	Morphine solution.	Permanganate solution.	Result.
8 control	1¼ lbs.	4 c.c.	None	Death in one hour and forty-two minutes.
9	1 lb.	4 c.c.	8 c.c.	Death in one hour and eight minutes.

Two experiments were performed upon cats, the poisons being used hypodermically.

No.	Weight.	Morphine solution.	Permanganate solution.	Result.
10 control	2.25 kils.	1.5 gm.	None	Death in thirty-seven minutes.
11	2.50 kils.	1.5 gm.	1.12	Death in thirty-five minutes.

The results in these three series of experiments are in entire accord; in the pigeons death was apparently hastened or produced by the permanganate; the rabbit that received the permanganate died in about two-thirds of the time that was required to kill the one which received no permanganate; the cat that had the alleged antidote also died a little sooner than its fellow, which was injected only with morphine sulphate. The results obtained by Reeb and his coadjutor may be explained by the supposition that the very loose tissue of the frog allowed the permanganate to permeate the body and the two substances to come in contact before absorption, although they were not injected into the same spot. At present both *à priori* reasoning and experimental evidence make it highly improbable that the permanganate has any influence upon a poison after its absorption.

Strychnine.

In order to test the antidotal value of potassium permanganate to strychnine, the first series of experiments was made similar to those with morphine,—namely, by adding the potassium permanganate solution to the strychnine. Rather strangely, I neglected to put in my notes the strength of the solution of strychnine used in these experiments, but believe it was $\frac{1}{20}$ of 1 per cent. The fact is, however, of little importance, since the solution used in the control and other experiments was the same.

Owing to the loss of time during filtration it was very difficult to determine how long the contact existed between the strychnine and potassium permanganate, the latter being used in excess, but so near as I can make out it was about five minutes. The decoloration of the permanganate solution is very pronounced at the end of one minute after the solutions have been poured together.

In three successive control experiments one cubic centimetre of the strychnine killed a pigeon in one minute; one-fourth of one cubic centimetre produced death in another pigeon in one minute; one-eighth of a cubic centimetre killed in five minutes. In the experiments with the filtrate, one pigeon survived three cubic centimetres of the filtrate

injected at once; a second pigeon received three cubic centimetres hypodermically of the filtrate, and two minutes later five cubic centimetres, and yet did not show marked evidences of strychnine poisoning. That, however, the strychnine was not completely destroyed was shown by the facts that after the evaporation of the filtrate, Professor Wormley was able to get a strychnine color reaction from the residue, and also that ten cubic centimetres of the filtrate injected into a very young rabbit caused death.

These experiments seem to demonstrate that the potassium permanganate has the power of destroying the alkaloid strychnine, but do not demonstrate that its action is sufficiently prompt and decisive to make it a reliable antidote. Further, the very skilful chemical studies of Professor Wormley show how limited the destructive influence of the permanganate is. He dissolved 100 milligrammes of strychnine sulphate in 10 cubic centimetres of water. He added 100 milligrammes of potassium permanganate filtered and evaporated to dryness: from the residue he extracted 62 milligrammes of undecomposed strychnine sulphate. In order further to test the matter, I made a series of experiments in which animals were given strychnine by the mouth.

Experiment.	Animal.	Time in Mins.	Dose, Strychnine Sulphate, 1-20 of 1 Per Cent. Solution; Permanganate, 4 Per Cent. Solution.	Result.
1	Dog, 8 kilos.	0	Strychnine, 8 c.c. Permanganate, 3 c.c. mixed and swallowed together.	No symptoms.
2	Same dog as in No. 1.	0.75	Strychnine, 8 c.c.	Death.
3	Dog, 13 kilos.	0	Strychnine, 10 c.c.	
		3	Permanganate, 3 c.c.	
		5		Violent general spasms.
		10		No spasms but rigidity.
		60		Better.
		75		Walk about all right.
4	Same dog as in No. 3.	0	Strychnine, 15 c.c.	
		1	Permanganate, 3 c.c.	
		6		Violent spasms.
		16		Died.
5	Dog, 12.5 kilos.	0	Strychnine, 10 c.c.	
		1	Permanganate, 3 c.c.	Recovery.
6	Dog, 10 kilos.	0	Strychnine, 10 c.c.	
		1	Permanganate, 3 c.c.	Recovery.

The experiment No. 1 of the present series, in which a dose of strychnine killed a dog in which the same dose given a couple of days before with the permanganate had caused no symptoms, shows that the latter salt has some antidotal power, although the later experiments prove that this power is limited.